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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,861	07/03/2002	Carlos Cordon-Cardo	55293-B-PCT-US/JPW/FHB	6709

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COOPER & DUNHAM LLP
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

EXAMINER	
UNGAR, SUSAN NMN	
ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
08/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/009,861	CORDON-CARDO ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *04 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114 including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to you 37 CFR 1.114. Applicant's submission filed are acknowledged and have been entered. Claim 28 has been canceled and claim 19 has been amended. An action on the RCE follows.

2 Claim 19 is pending and currently under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. It is noted that in the paper filed June 4, 2007, Applicant states that on May 24, 2007, Maria V. Marcci of the attorney's office had a telephone interview with Examiner Bridget Bunner concerning the outstanding rejections in this application, however, Examiner Bridget Bunner is not the Examiner of record and it is unclear why Applicant had that telephone interview. It is noted however, that the evidence submitted drawn to HERCEPTIN being the trade name for trastuzumab is convincing and amendment of the claim to recite trastuzumab is not found to be new matter.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 19 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed method for treating a research animal with androgen-independent prostate cancer, does not reasonably provide enablement for treating "a subject" with androgen-independent prostate cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims is drawn to a method for treating a subject afflicted with androgen-independent prostate cancer characterized by overexpression of Her-2/neu protein comprising a therapeutically effective amount of trastuzumab in conjunction with a therapeutically effective amount of paclitaxel, wherein treatment with trastuzumab and paclitaxel inhibits prostate cancer growth more than treatment with either trastuzumab alone or paclitaxel alone.

This means treating any subject including a human.

The specification teaches that herceptin alone does not effectively treat androgen-independent prostate cancer in xenograft models, but that herceptin in combination with paclitaxel resulted in cancer growth inhibition, wherein paclitaxel and herceptin cotreatment led to greater growth inhibition than was seen for the agents individually. The specification specifically teaches that "in these prostate cancer model systems, Herceptin.....has at least additive effect, in combination with paclitaxel, in .....androgen-independent tumors.

One cannot extrapolate the teaching of the specification to the scope of the claims because Morris et al (Cancer, 2002, 94:9890-986), whose authors include Inventor Howard I Scher of the instant Application, specifically teach that

alterations in Her-2 expression as a prostate tumor advances from androgen dependence to androgen independence have yet to be fully established although preliminary data suggest that expression is not uniform across disease states. The reference assayed the effects of HERCEPTIN alone and in combination with paclitaxel in both androgen-dependent and androgen-independent prostate cancer patients. Six patients with HER-2 negative disease received trastuzumab and paclitaxel and 9 patients who received both drugs were evaluable, wherein 5 patients experienced disease progression at or before the 12-week evaluation period, 3 patients had stable disease and 1 patient had a partial response. Six patients with androgen-independent, HER-2 positive disease were treated, wherein all progressed on single-agent trastuzumab at or before the 12 week landmark. Four patients received combination therapy, two patients had a partial response by PSA and two patients had disease progression (p. 983 col 1). The reference further states that "Although only patients in the HER-2 negative androgen-independent metastatic arm accrued to completion, we are reporting the pathology and the incomplete clinical data from the other arms because these results argue against seeking additional HER-2 positive patients until new methods of acquiring metastatic tissue to screen for HER-2 expression are developed. Given the plethora of studies using biologic agents, our experience suggests that screening for the targeted pathway must occur on tissue that represents the disease at the time of treatment, not at diagnosis." Critical to the instantly claimed invention the authors state that "Our clinical results reveal .....Although stable disease or partial responses were seen in 8 of 15 patients who received trastuzumab and paclitaxel, the value of adding trastuzumab to the chemotherapy regimen is uncertain because paclitaxel alone can induce response proportions in the 50%

range (p. 964, cols 1 and 2). Thus, it is clear that in this study that, Inventor Scher was unable to predictably determine that the therapeutic treatment would function as instantly claimed or to predictably determine whether or not treatment with the combination therapy in humans resulted in inhibition of prostate cancer growth more than treatment with either therapeutic alone. The reference then points to the difficulties in obtaining sufficient HER-2 positive androgen-independent patients in order to determine whether in fact the combination of trastuzumab and paclitaxel would be of value in the treatment of androgen-independent prostate cancer (see p. 985, col 1), wherein the problems are drawn to accurately identifying the population of antigen-independent prostate cancer patients that have HER-2 positive tumors that is drawn to problems of acquiring metastatic tissue from patients with prostate carcinoma patients. The reference further states that "even if metastatic tissue is available for screening, the most accurate means of determining the HER-2 status is controversial, nor is it established which method of HER-2 testing, if any, predicts a therapeutic response in patients with prostate carcinoma". Thus it is clear that even given "overexpression" the authors could not predict, nor had any tests that would aid in said prediction, which patients would have a therapeutic response in patients with prostate carcinoma. The authors conclude that although HER-2 remains a valid therapeutic target, the data from this trial suggests that trastuzumab is not active as a single agent for the treatment of patients with AI Her-2 negative disease and that further pursuit of patients with HER-2 positive disease for clinical testing is not feasible logistically using traditional immunopathologic methods. Future trials of biologic agents in patients with metastatic prostate carcinoma will require new techniques for assessing biological pathways in metastatic tissue and the assays used to test for these

pathways require further validation (p. 985, col 2). Given the above, it is clear that the instant claims are not enabled because Inventor Scher and co-authors clearly state that, two years after the priority date of the instant application that further development of trastuzumab for the treatment of patients with metastatic prostate carcinoma is not feasible until more reliable and practical methods of sampling metastatic disease are developed to identify patients with HER-2 positive tumors. If it is not possible to continue clinical trials of the combination treatment because of the lack of feasibility of identifying patients with HER-2 positive prostate tumors and the lack of results that would predictably indicate additive results for the HERCEPTIN/paclitaxel studies, it is clear that the instantly claimed method for a subject afflicted with androgen-independent prostate cancer characterized by overexpression of Her-2/neu protein is also not feasible and therefore was not enabled at the time the application was submitted. Further, Inventor Scher and coauthors made clear that the clinical trial demonstrated the uncertainty and therefore unpredictability of the value of adding trastuzumab to paclitaxel therapy for the treatment of androgen-independent prostate cancer in HER-2 overexpressing tumors. This finding apparently resulted in the termination of clinical trials drawn to adding HERCEPTIN to paclitaxel protocols for the treatment of androgen-independent prostate cancer.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the broadly claimed invention could be practiced with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

7. Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 is indefinite in the recitation of the term "overexpression". The claim is indefinite because the term "overexpression" is a relative term, The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

8. No claims allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley, can be reached at 571-272-0898. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this

application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
August 9, 2007